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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,434	01/10/2002	Jurgen Denecke	9052-84	1446

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EXAMINER	
KUBELIK, ANNE R	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 05/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,434	DENECKE ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 14-16* is/are pending in the application.

4a) Of the above claim(s) *8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 9-11 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-11 and 14-16 are pending.

2. This application contains claim 8 drawn to an invention nonelected with traverse in the response filed 21 July 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

3. Applicant's assurance that a new declaration will be sent is acknowledged. The objection will be maintained until the new declaration is received.

4. The abstract is not descriptive of the instant invention, which is a method of increasing secretory protein synthesis by transformation with a nucleic acid encoding BiP. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. The objection is repeated for the reasons of record as set forth in the Office action mailed 19 November 2003. Applicant's arguments filed 19 March 2004 have been fully considered but they are not persuasive.

Applicant urges that the abstract has been amended as suggested (response pg 6).

This is not found persuasive because the instant elected invention is not drawn to modifying signal transduction pathways.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. The objection to claims 2-7, 9, 11 and 14 because of informalities is withdrawn in light of Applicant's amendments to the claims.

7. The objection to claim 2 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in light of Applicant's amendments to the claim.

Claim Rejections - 35 USC § 112

8. Claims 1-7, 10-11 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing the capacity for secretory protein synthesis in a plant by transforming the plants with a nucleic acid that encodes tobacco BiP and plants and plant cells thereby obtained, does not reasonably provide enablement for a method of increasing the capacity for secretory protein synthesis in a plant by overexpressing BiP by any method and plants and plant cells thereby obtained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 19 November 2003. Applicant's arguments filed 19 March 2004 have been fully considered but they are not persuasive.

Applicant urges that the references cited in the previous Office action and the references cited by applicant in this reply show that the application of current technology requires routine effort not undue experimentation. Applicant urges that WO94/08012 provides guidance for overexpression of BiP and that well-known techniques in the art can be used to select a plant with the desired characteristics (response pg 7).

This is not found persuasive because WO94/08012 does not teach overexpression of BiP, but instead teaches overexpression of other proteins.

Applicant urges that they have enclosed as Appendix I a list of other nucleic acids listing various species and kingdoms encoding BiP known at the time of invention, and that BiPs are extremely conserved among plants (response pg 8).

This is not found persuasive because these other BiP are not taught by the specification, and no calreticulin DNAs are taught. The specification also fails to teach the ATPase domain of BiP.

Applicant urges that what matters is the amino acid sequence, because the degeneracy of the genetic code means that two genes encoding the same protein may have less that 50% homology (response pg 8).

This is not found persuasive because the specification fails to teach what amino acid substitutions to make when making BiP and calreticulin homologs.

Applicant urges that Denecke et al, 1991, shows that tobacco BiP can complement a yeast BiP mutant, showing that the function of BiP is extremely conserved; thus the instant invention would work with any eukaryotic BiP (response pg 8).

This is not found persuasive because the specification doe not teach any other BiP.

Applicant urges that BiP activity could be measured by the assay of LeBorgne-Castel, 1999 (response pg 8).

This is not found persuasive because the rejection is not drawn to methods of assaying BiP activity.

The specification also fails to teach a method of increasing the capacity for secretory protein synthesis in a plant by overexpressing BiP by any method other than transformation with a nucleic acid encoding BiP.

9. Claims 1-7, 9-10 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 19 November 2003. Applicant's arguments filed 19 March 2004 have been fully considered but they are not persuasive.

Applicant urges that the Written description Guidelines state that rejection of an original claim for lack of written description should be rare (response pg 8-9).

This is not found persuasive because this does not mean such a rejection should never be made.

Applicant urges that they have enclosed as Appendix I a list of other nucleic acids listing various species and kingdoms encoding BiP known at the time of invention, and that Denecke et al, 1991, shows BiPs are extremely conserved among plants (response pg 8).

This is not found persuasive because these other BiP are not described by the specification, and no calreticulin DNAs are described.

10. Claims 1-7, 9-11, and 14-16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.
The rejection is modified from the rejection set forth in the Office action mailed 19 November 2003, due to applicant's amendment of the claims. Applicant's arguments filed 19 March 2004 have been fully considered but they are not persuasive.

Claim 1 is indefinite in its recitation of "causing". It is not clear what one is doing here.

Claims 1, 3-7, 10-11 and 14-16 are indefinite in their recitations of "homologue".

Applicant urges that on pg 6 of the specification it states that "BIP includes any homologue thereof which has a significant degree of structural or functional similarity" (response pg 9-10).

This is not found persuasive because "homologue" is not defined, nor are "significant degree" or "structural or functional similarity" defined. How a homolog differs from BiP and calreticulin, in sequence and in function, is unclear. Furthermore, if the term "BiP" includes "homologues" why is the word even recited in the claim?

The following rejections are new, due to Applicant's amendment of the claims:

Claim 1 is indefinite in its recitation of "maintaining". For how long does the level have to be increased?

Claim 16 is indefinite in its recitation of "in an amount sufficient to accelerate the induction of PR gene expression". It is unclear what that amount is.

Claim Rejections - 35 USC § 102

11. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Crofts et al (1998, Plant Cell 10:813-823). The rejection is repeated for the reasons of record as set forth in the Office action mailed 19 November 2003. Applicant's arguments filed 19 March 2004 have been fully considered but they are not persuasive.

Applicant urges that claims are only anticipated if each and every element is in the prior art reference, and that prior at 15 December 1998, BiP and other ER chaperones were induced

during plant pathogen [sic] as a consequence of high secretory protein synthesis and there was no disclosure that Bip expression could lead to resistance. Applicant urges that BiP is induced prior to PR proteins and that Bip overexpression leads to accelerated PR gene induction, leading to an accelerated defense response (response pg 10-11).

This is not found persuasive because this is an inherent feature of the teachings of Crofts et al.

Applicant urges that one of the instant inventors is a co-author on this paper. Applicant urges that plants with increased pathogen resistance are not disclosed or taught, and no function for the complex is taught; the link between increased pathogen resistance and increased BiP levels was unappreciated (response pg 11).

This is not found persuasive because the claiming of a new use, new function or unknown property that is inherently present in the prior art does not necessarily make the claim patentable. See *In re Best*, 562 F.2d1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also In re Tomlinson, 363 F.2d 928, 150 USPQ 623 (CCPA 1966) (The claim was directed to a process of inhibiting light degradation of polypropylene by mixing it with one of a genus of compounds, including nickel dithiocarbamate. A reference taught mixing polypropylene with nickel dithiocarbamate to lower heat degradation. The court held that the claims read on the obvious process of mixing polypropylene with the nickel dithiocarbamate and that the preamble of the claim was merely directed to the result of mixing the two materials. "While the references do not show a specific recognition of that result, its discovery by appellants is tantamount only to finding a property in the old composition." 363 F.2d at 934, 150 USPQ at 628 (emphasis in original).).

12. Claims 1-4, 10-11 and 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Arora et al (1998, Physiol. Planta. 103:24-34). The rejection is repeated for the reasons of record as set forth in the Office action mailed 19 November 2003. Applicant's arguments filed 19 March 2004 have been fully considered but they are not persuasive.

Applicant urges that there is no mention of increased secretory synthesis causing a plant to maintain a level of BiP greater than the endogenous level; thus, the claims are not anticipated (response pg 11).

This is not found persuasive because Arora et la teach that water-stressing plants causes then to have levels of BiP that are over 5 times that of the endogenous level under non-stressful conditions (Figure 9). This increased level of BiP would be "maintained".

13. Claims 1-4, 10-11 and 14-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al (1992, Protoplasma 171:142-152). The rejection is repeated for the reasons of record as set forth in the Office action mailed 19 November 2003. Applicant's arguments filed 19 March 2004 have been fully considered but they are not persuasive.

Applicant urges that the elevation in BiP level is not thought to be a result of a mutation in the BiP gene itself but is a result of stress, and a method of increasing secretory protein synthesis or reducing the period of time for responding to pathogen attack is not disclosed (response pg 12).

This is not found persuasive because Zhang et al teach maize mutant plants in which BiP levels are at least five times that of the levels in non-mutant plants (Fig. 3); the instant claims do not limit the way BiP levels are incraesed. These plants would inherently have an increased capacity of secretory protein synthesis and would inherently have a reduced response time to pathogen attack.

Claim Rejections - 35 USC § 103

14. Claims 1-7, 10-11 and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crofts et al (1998, Plant Cell 10:813-823). The rejection is repeated for the reasons of record as set forth in the Office action mailed 19 November 2003. Applicant's arguments filed 19 March 2004 have been fully considered but they are not persuasive.

Applicant urges that BiP acts as a trigger to accelerate pathogen resistance and not merely as a consequence of pathogen challenge; Crofts at al does not teach or suggest the constructs used to transform the plants or the level of BiP produced in the present application. Applicant urges that the methods disclosed by Crofts et al refer to a method published by Leborgne-Castel et al after the priority date of the instant application; thus, Crofts et al is not enabling, and there is no suggestion to modify the teachings of Crofts et al (response pg 13).

This is not found persuasive because the sequence of tobacco BiP was known in the prior art, as were plant expression vectors and plant transformation. One of ordinary skill in the art could use the teachings of Crofts et al and the knowledge in the art to produce plants transformed with a nucleic acid encoding BiP. The teachings of Leborgne-Castel et al are not needed to practice the invention. Furthermore, one of skill in the art would use constructs having a strong constitutive promoter and a 3' termination sequence because the CaMV 35S promoter is the most commonly used promoter in plant molecular biological research and because 3' termination signals are required for correct expression of exogenous genes in plants.

15. Claims 9 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crofts et al as applied to claim s 1-7, 10-11 and 14-15 above, and further in view of Denecke et al (1995, Plant Cell 7:391-406). The rejection is repeated for the reasons of record as set forth in the

Office action mailed 19 November 2003. Applicant's arguments filed 19 March 2004 have been fully considered but they are not persuasive.

Applicant urges that Crofts et al is not enabling for the present claims and there is no motivation to combine Crofts et al with Denecke et al because Crofts et al is concerned with the function of the BiP-calreticulin complex and not with pathogen resistance (response pg 13-14).

This is not found persuasive because Crofts et al sate that it is the level of BiP that influences the level of the BiP-calreticulin complex and Denecke showed that BiP levels are increased in response to salicyclic acid.

16. Claims 1-4, 6, 10-11 and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coughlan et al (US Patent 6,171,864, filed July 1996). The rejection is repeated for the reasons of record as set forth in the Office action mailed 19 November 2003. Applicant's arguments filed 19 March 2004 have been fully considered but they are not persuasive.

Applicant urges that '864 does not disclose plants transformed with a vector encoding calreticulin, and there is no suggestion to motivation to modify the teachings of this reverence or combine it with any other citation to obtain the instantly claimed method (response pg 14).

This is not found persuasive because Coughlan et al teach plant cells transformed with a vector encoding calreticulin in claims 13-14 and Coughlan et al suggests regenerating those plant cells into plants in column 14, lines 66-67.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (571) 272-0547.

Anne R. Kubelik, Ph.D.
May 6, 2004